

**Amendments to the Drawings:**

The drawing sheet attached in connection with the above-identified application containing Figure 1 is being presented as a new formal drawing sheet to be substituted for the previously submitted drawing sheet. The drawing Figure 1 has been amended. Appended to this amendment is an annotated copy of the previous drawing sheet which has been marked to show changes presented in the replacement sheet of the drawing.

The specific change which has been made to Figure 1 is to re-label the top portion of Figure 1(B) to read “hPRLA”. Support for this change may be found in paragraph [0022] which correctly identifies the contents of Figure 1(B) as a “hPRLA-IL-2 fusion protein.”

**REMARKS****I. Introduction**

Receipt of a non-final office action dated October 21, 2005 is acknowledged. In the action, claims 1, 3-6, 22, 28, 35-39, 45-46, 51-54 and 56 are rejected for allegedly failing to meet the written description requirement, and claim 33 is rejected as allegedly indefinite. Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

**II. Amendments to the Specification**

In this response, applicants amended paragraphs [0020], [0026], and [0042] of the specification and submitted a new sequence listing (Appendix A).

**III. Status of the Claims**

Applicants cancelled claims 33, 56, and 58-60, amended claims 1, 28, 29, 34, 45-47 and 51, and added new claims 61-71. Although claims 58-60 were previously presented in a March 22, 2005 response to a final office action, it is unclear if they have been entered. Nevertheless, for purposes of claim numbering and status identifiers, applicants treat claims 58-60 as if they had been entered and submit the newly added claims starting with claim number 61. Because the foregoing amendments do not introduce new matter, entry thereof by the examiner is respectfully requested.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier. Applicants note that the cancellation of claims does not constitute acquiescence in the propriety of any rejection set forth by the examiner. Applicants reserve the right to pursue the subject matter of the canceled claims in subsequent divisional applications.

Upon entry of this amendment, claims 1, 3-6, 22, 28-29, 34-39, 45-47, 51-54, and 61-71 will be under examination.

**IV. Response to Issues Raised by Examiner in Outstanding Office Action****a. Claim Rejections - 35 U.S.C. § 112, First Paragraph**

Claims 1, 3-6, 22, 28-29, 33-39, 45-47, 51-54, and 56 are rejected under 35 U.S.C. § 112, first paragraph for lack of written description. In particular, the examiner asserts that “[t]he written description in this case has only set forth a method of treating a cancer comprising the administration of a prolactin receptor antagonizing domain of SEQ ID No: 1 with a substitution at amino acid position 157 or a prolactin receptor antagonizing domain wherein the domain comprises a G129R mutation; and a positive immunomodulatory domain, wherein the domain is a cytokine . . . .” Office Action, p. 2. Applicants respectfully traverse this ground for rejection.

The specification adequately describes methods of treating cancer and methods for inducing an immune response with a protein that comprises a receptor antagonizing domain that can be a prolactin antagonist domain or a growth hormone antagonist domain. See, for example, paragraphs [0041] and [0051] of the published application.

Nevertheless, in the interest of expediting prosecution, applicants amended the claims to recite that the prolactin antagonist domain and the growth hormone antagonist domain comprise an amino acid substitution at position 129 or position 120 in hPRL or hGH, respectively. One of skill in the art would know, based on the teachings in the present specification and prolactin and growth hormone sequence information known in the art at the time of filing, what amino acids would be suitable substitutions in position 129 of hPRL or position 120 of hGH to obtain a prolactin or growth hormone antagonist. See, for example, paragraphs [0044] to [0046], which describe that bulky side-chain amino acid substitutions, including arginine would result in an antagonistic form of the protein, as well as conservative substitutions of the receptor antagonizing domains. Furthermore, paragraph [0046] lists various amino acid residues and names conservative substitutions of arginine. Accordingly, a skilled artisan would know which amino acid substitutions would be suitable modifications at position 129 of hPRL or position 120 of hGH, in view of the disclosure in the present invention.

Furthermore, with regard to the prolactin receptor antagonizing domain of SEQ ID NO: 1 with a substitution at position 157, applicants wish to point out that SEQ ID NO: 1 includes a leader sequence and that this leader sequence is not present in wild-type hPRL. Thus, if the leader sequence were deleted, as it is in hPRL, position 129 is a glycine. And for clarity sake, applicants submit herewith a new sequence listing which includes a SEQ ID No. 34, drawn to a hPRL sequence. This sequence therefore does not include the leader sequence and therefore begins with the Leucine well known to a person of skill in the art as the first amino acid in PRL. For example, see Growth Hormone, edited by Harvey, et al., CRC Press, p. 7-8 (1995), submitted herewith in Appendix B. Support for this sequence can be found in paragraph [0042], which provides that in one embodiment of the present invention, the PRLA contains a substitution at position 129 from Glycine to Arginine. The new SEQ ID NO. 34 provides the sequence understood by a person of skill in the art to relate to the present invention.

In other words, a person of skill in the art reading the specification would understand that SEQ ID No. 1 includes a leader sequence that is not present in hPRL. Table 1 in the application shows the invariability of G129 across multiple species and the PRLA domain in one embodiment described in the specification contains an arginine substitution at position 129 and is provided in SEQ ID No. 34.

Accordingly, applicants respectfully request reconsideration and withdrawal of the written description rejection.

**b. Claim Rejections - 35 U.S.C. § 112, Second Paragraph**

Claims 33 and its dependents are rejected by the Examiner under 35 U.S.C. § 112, second paragraph as being allegedly indefinite. The Examiner asserts, "The sequence listing submitted 3/23/2001 indicates that amino acid position 129 of SEQ ID No: 1 is a Glutamic acid (Glu) and is not Glycine (Gly)" and therefore, "it [is] indefinite what the applicant is intending to claim." Office action, p. 5. As indicated above, a new sequence listing is submitted herewith which includes a prolactin antagonist without the leader sequence. This sequence listing provides a Gly to Arg substitution at position 129. Thus, applicants respectfully request reconsideration and withdrawal of the rejection.

**CONCLUSION**

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

Examiner Yaen is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

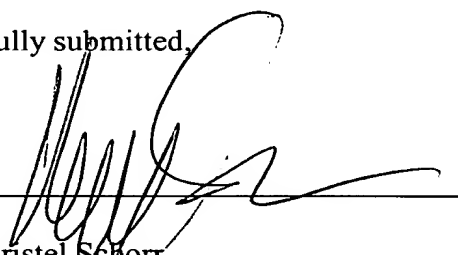
The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

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Respectfully submitted,

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